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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/173,821	10/16/98	RUDLAND P	32040PCTUSA-

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EXAMINER	
KAUSHAL,S	

ART UNIT	PAPER NUMBER
1633	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/173,821	Applicant(s) RUDLAND et al
	Examiner Sumesh Kaushal	Group Art Unit 1633

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-24* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-24* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The instant application is continuation of PCT/GB97/01063 filed 04/17/97 which claims priority to a foreign application UK 9607953.8 filed on 4/17/96.

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17 is rejected under 35 U.S.C. 101 because claim is drawn to non-statutory subject matter. Claims 17 is to transgenic mammal, which encompasses humans. It is PTO policy not to allow claims to humans (1077 O.G. 24 April 1987). The insertion of non human before transgenic mammal(s) will overcome this rejection.

Claim Objections

2. Claim 12 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other multipledependent claim. See MPEP § 608.01(n). Accordingly, the claim 12 has not been further treated on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 9 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The application discloses [cell lines having ECACC accession number 969275 and 97032720] that is encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public, even though the deposit has been apparently made. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological

material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

Claims 1-11, 13, 17 and 21-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for i) cell line derived from transgenic rat comprising: B2LT1 rat mammary cells (MMTV-SV40tsA58) and NF2 rat brain cells (NS-LtsA58) ii) transgenic rats comprising: MMTVLTR-TGFα and MMTVLTR-C-erb-B-2, does not reasonably provide enablement for any and all transgenic cell lines and/or transgenic animals comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims are drawn to a cell line derived from a transgenic animal comprising a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene and a cell specific promoter. The cell lines are derived from neuronal cells (with NF-L promoter), mammary cells (with MMTV promoter), liver cells or kidney cells wherein the conditional oncogene, transforming gene or immortalizing gene is SV40tsA58 gene and cell cycle affecting genes is a C Erb β-2 or TGF-α gene. Claims are also drawn to a transgenic mammal whose germ cells and somatic cell contain a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene and

a cell type specific promoter, wherein the cell cycle affecting gene is a is a C Erb β-2 or TGF-α gene. Claims are drawn to a method of producing transgenic animals. Furthermore claims are also drawn to a cell line and/or a tissue derived from a transgenic mammal and a method of providing cell line or tissue by culturing a somatic cells obtained from a transgenic animal.

The specification teaches the super ovulation of female rats by continuously infusing Follicle Stimulating Hormone (FSH) using a mini pump and micro injection of DNA into the pronuclei of single cell rat embryo (page 21-24. App. Spec). The specification teaches the development and breeding of the mammary targeted MMTVLTRtsA58U19 line of transgenic rats (page 25, table-1, page 28, table-2). Furthermore, the specification also teaches the development and breeding of neuronal targeted NF-Lts58Uδt line of transgenic rats (page 30 table-3, page 28, table-2). In addition the specification demonstrated the cell surface marker of mammary specific (on B2LT1 cells) and neuronal specific (on NF2C cells) marker on cell lines derived from transgenic rats (page 34, table-4; page 37, table-4). The specification also teaches generation and breeding of mammary targeted MMTVLTR-TGFα and MMTV-c-erb-β-2 transgenic rats which resulted in lesions in mammary tissue (page 50 table-6). However, the specification fails to provide guidance to make and use, any and all transgenic cell lines derived from any and all transgenic mammals comprising a conditional, transforming gene or immortalizing gene or a cell cycle affecting gene and cell type specific promoter. The specification is not enabled for the method of producing any and all transgenic mammals because specification fails to provide guidance to make and use non-rat transgenic mammals using the continuous supply of FSH. The specification is not enabled for any and all transgenic mammals and cell lines derived thereof because it fails to provide guidance to make and use any and all conditional oncogenes, transforming genes, immortalizing genes or cell cycle effecting genes operably linked to any and all cell type specific promoters. Although, the specification teaches the making of a neuronal and mammary cell line it fails to make and use of any and all liver and/or kidney cell lines.

The state of transgenic art at the time of filing was such that transgene expression and physiological consequences of transgene products in non-murine mammals are not always accurately predicted of transgenic murine studies because cis elements are controlled differently by various transacting factors in the genome of different species (Wall RJ Theriogenology 45:57-68, 1996; see page 62 par.1 lin.5, page 61 table-1). It is important to note that, the scope of the claims include not only rats but other mammals including whales, pigs, cows and monkeys. Thus, considering the state of transgenic art and the guidance provided in the specification, the skilled artisan at the time of filing would be lacking a reasonable expectation of success for making any and all transgenic cell lines derived from any and all transgenic mammals, comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters, without an undue amount of experimentation for the breadth of the claims.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-8, 10, 14-16 and 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1-8 and 10 recite "derived" which fails to define the metes and bounds of claimed invention.

Claims 14-16 recite the limitation "regular supply" in claim 14, line 4. There is insufficient antecedent basis for this limitation in the claim.

Claim 16 recites "from 2mg to 8mg" which render this claim indefinite because duration and intervals of such a dose are not defined.

Claims 21-24 recites the limitation "the invention" in claim 21, line 3 claim 22 line 3, claim 23 line 4, claim 24 line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 17 and 19-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Leder et al (US Pat No. 5087571, 1992). Leder et al teaches method of providing a cell line from a transgenic non-human mammal encoding a transforming oncogne operably linked to mammary specific promoter MMTVLTR (col.4 line 13-22, col.9 line 11-20). Leder et al also teaches the use of transgenic animals for testing a material suspected of being a carcinogen (col.8 line 50-68). The cited art also teaches a method of testing a material for its ability to confer protection against the development of neoplasms using transgenic animals (col.9 line 1-9). Thus, the cited art clearly anticipated the invention of instant claims.

Claims 1, 3 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Reeben et al (Biochem. Biophy. Res. Com. 192(2):465-470, 1993). Reeben et al teaches tissue specific

expression of rat light neurofilament (NF-L) promoter to drive the expression of a reporter gene (page 467, para.1, fig-1, page 468, fig-3). The cited art anticipated the claimed invention because the product claim is not distinguished from the prior art by the method of making it. The elements i) and ii) of claim 1 are not required to be either linked to each other or be linked to a transgene in the cell. Furthermore, elements i) and ii) of claim 1 reads upon any mammalian cell.

Claims 1, 3, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Noble at al (WO 91/13150, 1991). Noble et al teaches transgenic animals and tissue specific cell lines obtained form the animal body, wherein the cell line comprises SV40tsA58 immortalizing gene (fig-1; page 34, line 1-20, page 35-40, page 50, line 19, page 53, line 22, page 56, line 16, page 59, example-3, page 61 example-4 page 64, example-5 page 69, example-6, page 74, example-7). Thus, Noble et al anticipated the invention of instant claim. The product claim is not distinguished from the prior art by the method of making it. The elements i) and ii) of claim 1 are not required to be either linked to each other or be linked to a transgene in the cell. Furthermore, elements i) and ii) of claim 1 reads upon any mammalian cell.

Claims 1-5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Moses JH (Br. J. Cancer. 69(21):1, 1994) or Stocklin et al (J. Cell Bio. 122(1):199-208, 1993). Moses teaches a tarnsgenic mice expressing a gene encoding hu TGF-a under the control of MMTV enhancer/promoter in mammary cells (page 1, s1). Stocklin et al teaches a transgenic mice wherein the human C-erbB-2 is operably linked to MMTV enhancer/promoter sequence wherein the transgene is expressed in kidney, lung, mammary, muscle, spleen, brain and liver cells (page 200, col.2 para.5, page 201, fig-1, col.2 para 2-3, page 202, table-II). Thus, the cited art(s) anticipated the invention of instant claims. The product claim is not distinguished from the prior art by the method of making it. The elements i) and ii) of claim 1 are not required to be either linked to each other or

be linked to a transgene in the cell. Furthermore, elements i) and ii) of claim 1 reads upon any mammalian cell.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noble et al (WO 91/13150, 1991) in view of Stocklin et al (J. Cell Bio. 122(1):199-208, 1993), and further in view of Reeben et al (Biochem. Biophy. Res. Com. 192(2):465-470, 1993). Noble et al teaches making of cell lines from the tissue of a non human transgenic animal encoding for SV40tsA58 gene (page 45, line 25-28, page 46, line 1-29, page 47, line 9-12, page 31 line 24-29). However, Noble et al does not teaches the regulation of a transgene using a cell type specific promoter. Stocklin et al teaches a transgenic mice wherein the transforming human c-erbB-2 is operably linked to MMTV enhancer/promoter sequence wherein the transgene is expressed in kidney, lung, mammary, muscle, spleen, brain and liver cells (page 200, col.2 para.5, page 201, fig-1, col.2 para 2-3, page 202, table-II). Reeben et al teaches tissue specific expression of rat light neurofilament (NF-L) promoter to drive the expression of a reporter gene in a transgenic mice (page 467, para.1, fig-1). Thus, Noble et al teaching the making of tissue specific cell lines from a trangenic animal, Stocklin et al teaching the use of MMTV promoter and Reeben et al teaching the use of NF-L to derive tissue specific

expression of a transforming gene, it would have been obvious to one with ordinary skill in the art at the time of invention to make cell lines from a transgenic rat encoding a tissue specific promoter operably linked to SV40tsA58. One would have been also motivated to derive a tissue cell line from a transgenic animal because these cell harbors the characteristic of tissue specific markers.

Claims 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hammer et al (US Pat. No. 5489742, 1996) in view Leder et al (US Pat No. 5087571, 1992). Hammer et al teaches a method for preparing transgenic rats, by super ovulating a female rat by continuous supply of FSH hormone using a mini-pump followed by the introduction of a transgene into the fertilized egg (col.15 line 60-67, col.1, line 1-17). However, Hammer et al does not teaches a method, where the transgenic animals incorporate a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene. Leder et al teaches a transgenic mice encoding a transforming oncogne operably linked to mammary specific promoter MMTVLTR (col.4 line 13-22, col.9 line 11-20). Thus, Hammer et al teaching a method of producing transgenic rats by superovulating female rats by continuously supply FSH and Leder et al teaching a transgenic mice with a transforming oncogne, it would have been obvious to one with ordinary skill in the art at the time of invention to produce transgenic rats by super ovulating female rats, wherein the transgenic rat express an onocgne. One would have also been motivated make female rat super-ovulate by continuous supply FSH because rat have traditionally been found to be difficult to effect superovulation (Hammer et al, col.7 line 29-43). Furthermore, in addition to transgenic mice, a transgenic rat model would provide two fold experimental approach for the same transgene.

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hammer et al (US Pat. No. 5489742, 1996) in view of Moses JH (Br. J. Cancer. 69(21):1, 1994) or Stocklin et al (J. Cell Bio. 122(1):199-208, 1993). Hammer et al teaches a method for preparing transgenic rats by subjecting a female rat to hormonal conditions effective to promote superovulation, followed

by fertilizing eggs, and introduction of a transgene into the fertilized eggs, wherein female rats are superovulated by a continuous infusion of follicle stimulating hormone (FSH) using a mini-pump (col.15 line 60-67, col.1, line 1-17). Moses teaches a tarnsgenic mice expressing a gene encoding hu TGF-a under the control of MMTV enhancer/promoter (page 1, s1). Stocklin et al teaches a transgenic mice wherein the human c-erbB-2 is operably linked to MMTV enhancer/promoter sequence (page 200, col.2 para.5, page 201, fig-1). Thus, Hammer et al teaching the method of making of a transgenic rat, Moses or Shocklin teaching the making of transgenic mice expressing TGF-a and c-erbB-2, it would have been obvious to one with ordinary skill in the art to a make a transgenic rat expressing TGF-a and c-erbB-2. One would have been also motivated to have a transgenic rat expressing the same transgene as a transgenic mice because rats are widely used in biomedical research. Furthermore, in addition to transgenic mice, a transgenic rat would provide two fold experimental approach for the same transgene studies.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM . If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brian Stanton Ph.D. can be reached on (703) 308-2801. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

Sumesh Kaushal
Art Group 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL ATTACHMENT

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address. (See 37 C.F.R. § 1.803).

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.